

**REMARKS**

Claim 2 has been cancelled, without prejudice.

Claim 1 has been amended to recite "[a] vector or plasmid comprising an isolated DNA encoding vitamin B<sub>6</sub> phosphate phosphatase selected from the group consisting of:

(a) a DNA sequence of SEQ ID NO:9;

(b) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity and hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof;

(c) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity, wherein said polypeptide is at least 70% identical to the amino acid sequence of SEQ ID NO:10;

(d) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity and is at least 70% identical to the DNA sequence of SEQ ID NO:9; and

(e) a degenerate DNA sequence of any one of (a) to (c)." Support for this amendment is found in the specification at, for example, page 3, lines 8-22; in Examples 1-2; and in original claims 1 and 2. See *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (I) (8<sup>th</sup> ed. Rev. 5, August 2006, pp. 600-92 and 600-84).

Claim 4 has been amended to recite "[a] recombinant microorganism of the genus *Sinorhizobium* or *Escherichia*, capable of producing vitamin B<sub>6</sub> from vitamin

B<sub>6</sub> phosphate, wherein said microorganism is transformed with a DNA encoding vitamin B<sub>6</sub> phosphate phosphatase selected from the group consisting of:

- (a) a DNA sequence of SEQ ID NO:9;
- (b) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity and hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof;
- (c) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity, wherein said polypeptide is at least 70% identical to the amino acid sequence of SEQ ID NO:10;
- (d) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity and is at least 70% identical to the DNA sequence of SEQ ID NO:9; and
- (e) a degenerate DNA sequence of any one of (a) to (c).” Support for this amendment is found in the specification at, for example, page 3, lines 8-22; in Examples 1-2; and in original claim 1. (*Id.*).

Claim 11 has been amended to depend from claim 1 instead of cancelled base claim 2.

Claims 14 and 15 have been added. Support for these claims is found in the specification at, for example, page 2, line 22 - page 4, line 9; SEQ ID NOs:9 and 10; and in original claim 1.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

**Objections:**

The Examiner objected to claim 1, parts (a), (c), and (d) because of the recitation "sequence represented in." (Paper No. 20070206 at 4). The Examiner suggested amending the phrase to recite "sequence of." (*Id.*).

The Examiner also objected to claim 1, parts (b), (c), and (d) because of the recitation "sequence which encodes." (*Id.*). The Examiner suggested amending the phrase to recite "sequence encoding." (*Id.*).

The Examiner further objected to claim 1, part (b) because of the recitation "fragment of thereof." (*Id.*). The Examiner suggested amending the phrase to recite "fragment thereof." (*Id.*).

As suggested by the Examiner, and with a view towards furthering prosecution, claim 1 has been amended to recite "sequence of," "sequence encoding," and "fragment thereof," where appropriate. In view of these amendments, it is believed that the objections are rendered moot. Accordingly, withdrawal of the objections is respectfully requested.

**35 U.S.C. § 112, Second Paragraph, Rejection:**

Claims 1-2 and 4-7 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. (Paper No. 20070206 at 6).

In making the rejection, the Examiner asserted that the phrase "hybridizes under standard conditions" renders the claims indefinite. (*Id.*). The Examiner also asserted that "the specification does not define what conditions constitute 'standard conditions' for hybridization." (*Id.*). The Examiner further asserted that "[w]hile page 3 attempts to describe 'standard conditions' for hybridization, the description is merely

exemplary and not a clear definition. In the art the meaning of the term 'standard' hybridizing conditions varies widely depending on the individual situation and the person making the determination. Therefore, it is not clear to the Examiner as to what hybridization conditions are encompassed in the above phrase." (*Id.* at 6-7).

Initially, we note that claim 2 has been cancelled, without prejudice. With a view towards furthering prosecution, claims 1 and 4 (from which claims 5-7 depend) have been amended to replace the phrase "standard conditions" with the phrase "stringent hybridization and stringent washing conditions." The specification as filed provides details as to how this phrase is to be interpreted, *see, e.g.*, page 3, lines 8-22. For a specific example of these hybridization procedures, the specification discloses that:

The hybridization solution contains 50% formamide, 5xSSC (10xSSC is composed of 87.65 g of NaCl and 44.1 g of sodium citrate in 1 liter), 2% blocking reagent (Roche Diagnostics, Tokyo, Japan), 0.1% N-lauroylsarcosine, and 0.3% sodium dodecyl sulfate (referred as to SDS hereinafter). Hybridization can be done overnight at 42°C. and then washing twice in 2xSSC containing 0.1% SDS for 5 min at room temperature and twice in 0.1xSSC containing 0.1 % SDS for 15 min at 50° C. to 68° C. Detection can be done as indicated by manufacturer. [Specification, page 3, lines 16-22].

In view of the amendments and the disclosure in the specification for the particulars of the high stringency wash and hybridization, it is respectfully submitted that one skilled in this art would readily understand the scope of the claims.

For the reasons set forth above, it is believed that the rejection of claims 1-2 and 4-7 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

**§112, First Paragraph Rejections:**

**1. Deposit Requirement**

Claims 5-6 and 9-10 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. (Paper No. 20070206 at 4). In making the rejection, the Examiner asserted that "[t]he invention appears to employ novel microorganisms (*S. meliloti* IFO 14782/pVKPtacpdxP and *E. coli* JM109/pKKpdxP) comprising a gene encoding B6 phosphate phosphatase. Since the microorganisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The recited microorganisms have not been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. [§] 112 may be satisfied by a deposit of the microorganisms. The specification does not disclose a repeatable process to obtain the microorganisms and it is not apparent if the microorganisms are readily available to the public. Accordingly, it is deemed that a deposit of these microorganisms should have been made in accordance with 37 CFR 1.801-1.809." (*Id.*).

Initially, we note that the *Sinorhizobium meliloti* IFO 14782 (DSM 10226) strain was deposited under the terms of the Budapest Treaty at Deutsche Sammlung von Mikroorganismen und Zeilkulturen GmbH (DSMZ) in Gottingen, Germany under the Deposit No.: DSM 10226, on September 4, 1995.<sup>1</sup>

For the *Sinorhizobium meliloti* IFO 14782 (DSM 10226) deposit, the following statements are provided upon information and belief:

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<sup>1</sup> Attached as Exhibit 1 is a certificate from the DSMZ confirming that strain *Sinorhizobium meliloti* IFO 14782 (DSM 10226) has been deposited under the terms of the Budapest Treaty.

During the pendency of this application, access to the deposit will be afforded to the Commissioner upon request.

All restrictions imposed by the depositor on the availability to the public of the above-referenced deposited material will be irrevocably removed upon the granting of a patent.

The deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer.

The deposit will be replaced if it should ever become unavailable.

Thus, although not necessary to comply with §112, first paragraph, it is respectfully submitted that the application fully complies with the deposit requirements as set forth in 37 CFR § 1.808.

Furthermore, contrary to the Examiner's assertion, we note that the specification discloses a repeatable process to obtain *Sinorhizobium meliloti* IFO 14782 carrying plasmid pVKptacpdxP and *E. coli*. JM109 carrying plasmid pKKpdxP. (See Specification at page 3, line 26 to page 4, line 25). We also note that the plasmid pVKptacpdxP consists of pVK100, which is a well known and commercially available vector, and the fragments ptac and pdxP prepared from pKK-pdxP. The designation pVK100 stands for a cosmid cloning vector having a broad host range, and it can be purchased from Deutsche Sammlung von Mikroorganismen und Zeilkulturen GmbH (DSMZ) in Gottingen, Germany. (See, e.g., DSM No. 7141 at <http://www.dsmz.de/plasmids/pls07141.htm>). pVK100 has also been described in several articles. Attached as Exhibit 2, for the Examiner's convenience, is a printout

from the Internet demonstrating that plasmid pVK100 is readily available. The latter vector pKK-pdxP consists of the pdxP fragment and pKK223-3 as shown in Figure 2 and described in the specification at page 3, line 26 to page 4, line 25. Vector pKK223-3 is also commercially available (see Exhibit 3). Further, the DNA sequence of the pdxP gene corresponds to SEQ ID NO: 9 as described in Example 1 of the specification.

Thus, the specification discloses a repeatable process to obtain *Sinorhizobium meliloti* IFO 14782 carrying plasmid pVKptacpdxP and *E. coli*. JM109 carrying plasmid pKKpdxP starting from commercially available materials and/or using material fully described in the specification. Accordingly, the rejection has been rendered moot and should be withdrawn.

## **2. Enablement**

Claims 1-2 and 4-7 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. (Paper No. 20070206 at 7). In making the rejection, the Examiner acknowledged that the specification "[is] enabling for an isolated DNA with SEQ ID NO: 9, which encodes a polypeptide vitamin B6 phosphate phosphatase enzyme of SEQ ID NO: 10 isolated from *S. meliloti*." (*Id.*).

The Examiner, however, asserted that "the specification ... does not reasonably provide enablement for any DNA that is 70% identical to SEQ ID NO: 9 or any DNA encoding a protein having phosphatase activity and having at least 70% identity to SEQ ID NO: 10 or any fragments thereof or any DNA which hybridizes under any standard conditions including low stringency conditions to SEQ ID NO: 9 and encodes a polypeptide having phosphatase activity." (*Id.*).

Initially, we note it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry his/her burden, the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370. It is well established that claims must be separately analyzed. *Ex parte Jochim*, 11 USPQ2d 561 (BPAI 1988).

With a view towards furthering prosecution, claim 2 has been cancelled, without prejudice and claims 1 and 4 (from which claims 5-7 depend) have been amended to replace the phrase "standard conditions" with the phrase "stringent hybridization and stringent washing conditions." The specification as filed provides details as to how this phrase is to be interpreted, see, e.g., page 3, lines 8-22. For a specific example of these hybridization procedures, the specification discloses that:

The hybridization solution contains 50% formamide, 5xSSC (10xSSC is composed of 87.65 g of NaCl and 44.1 g of sodium citrate in 1 liter), 2% blocking reagent (Roche Diagnostics, Tokyo, Japan), 0.1% N-lauroylsarcosine, and 0.3% sodium dodecyl sulfate (referred as to SDS hereinafter). Hybridization can be done overnight at 42°C. and then washing twice in 2xSSC containing 0.1% SDS for 5 min at room temperature and twice in 0.1xSSC containing 0.1 % SDS for 15 min at 50° C. to 68° C. Detection can be done as indicated by manufacturer. [Specification, page 3, lines 16-22].

We note that the phrase "hybridizes under stringent hybridization and stringent washing conditions" is an art-recognized phrase that one skilled in the art would understand, even without further guidance from the specification. However, as discussed above, the specification as filed discloses how this term is to be interpreted.



It is respectfully submitted that one skilled in the art armed with the presently amended claims, the specification, and the knowledge in the art would very quickly be able to determine that Applicants enabled the full scope of the presently claimed invention. With these amendments, it is respectfully submitted that the Examiner's concerns regarding the scope of the claims are rendered moot.

Moreover, as is well accepted, even a "considerable amount" of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance. MPEP § 2164.05 and *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In addition, "a patent need not teach, and preferably omits, what is well known in the art." MPEP § 2164.01 (8<sup>th</sup> ed. Rev. 5, August 2006, p. 2100-187) citing *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

In this regard, we note that the specification provides ample disclosure sufficient to inform a skilled artisan that the Applicants enabled the currently claimed vectors, plasmids, and recombinant microorganisms. For example, the specification discloses two examples and four detailed Figures that provide sufficient instruction to one skilled in the art on how to make and use the currently claimed recombinant microorganism, vector, or plasmid encoding vitamin B<sub>6</sub> phosphate phosphatase.

Thus, identifying a recombinant microorganism capable of encoding vitamin B<sub>6</sub> phosphate phosphatase according to the amended claims is a matter of

applying the disclosure in the specification of how to make such microorganisms and testing the vitamin B<sub>6</sub> production of the microorganisms compared to *Sinorhizobium meliloti* IFO 14782. (See Table 6 of the Specification). It is respectfully submitted that such activity is not undue experimentation.

For the reasons set forth above, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

**Rejection under 35 U.S.C. § 102(b):**

Claim 1 was rejected under 35 USC § 102(b) as anticipated by Capela *et al.*, GenBank Accession No. AL591783 (nucleic acid), August 2001, and GenBank Accession No. Q92SG4 (protein), December 2001) ("Capela"). (Paper No. 20070206 at 11).

For the reasons set forth below, the rejection, has been rendered moot.

Capela discloses the isolation of a nucleic acid (GenBank Accession No. AL591783) and a protein (GenBank Accession No. Q92SG4).

In making the rejection, the Examiner asserted that Capela "teach[es] a DNA, which encodes a putative oxidoreductase type protein, [that] is 99.5% identical to SEQ ID NO: 9 of the instant application, inherently a vitamin B<sub>6</sub> phosphate phosphatase protein." (Paper No. 20070206 at 11). The Examiner further asserted that "[s]ince, the broadest reasonable interpretation of claim 1 is any DNA sequence [that] would hybridize at low stringency hybridizing conditions ... to SEQ ID NO: 9 ... Capela *et al.* anticipates claim 1 of the instant application." (*Id.*).

As is well settled, anticipation requires "identity of invention." *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply*, 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Each and every element recited in a claim must be found in a single **prior art reference** and arranged as in the claim. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir 1984). "Moreover, it is incumbent upon the Examiner to **identify wherein each and every facet** of the claimed invention is disclosed in the applied reference." *Ex parte Levy*, 17 USPQ2d 1461, 1462 (BPAI 1990). The Examiner is required to point to the disclosure in the reference "**by page and line**" upon which the claim allegedly reads. *Chiong v. Roland*, 17 USPQ2d 1541, 1543 (BPAI 1990). This the Examiner has not done.

Initially, we note that claim 1 has been amended to recite "[a] vector or plasmid comprising ....." Capela, as acknowledged by the Examiner, is **devoid of any disclosure of a vector or plasmid**. (See Paper No. 20070206 at 12) ("Capela et al. do not teach a vector comprising said sequence ....").

Accordingly, Capela does not disclose each and every element of claim 1. For this reason alone, it is respectfully submitted that the rejection fails to present a *prima facie* case for anticipation and must be withdrawn.

Furthermore, the Examiner fails to identify where in AL591783 it is disclosed that the translation product defined by the polynucleotide sequence encodes "a vitamin B<sub>6</sub> phosphate phosphatase." The Examiner merely asserted that Capela "teach[es] a DNA, which encodes a putative oxidoreductase type protein, [that] is 99.5% identical to SEQ ID NO: 9 of the instant application, **inherently a vitamin B6**

***phosphate phosphatase protein.***” (Paper No. 20070206 at 11) (emphasis added).

We note that a nucleotide sequence ***is not and can never be*** “inherently” a protein.

The Examiner does not - and cannot - identify where in Capela it is stated, or even suggested, that “a DNA encoding a vitamin B<sub>6</sub> phosphate phosphatase is known in the art.” The Examiner also suggests that Capela discloses “a putative oxidoreductase type protein.” (*Id.*). However, as is shown from GenBank Accession No. AL591783 and GenBank Accession No. Q92SG4 (Uniprot). Capela does not indicate any function of the polypeptide sequence, and it is simply characterized as a “hypothetical protein.” See GenBank Accession No. Q92SG4.

Indeed, the Examiner’s conclusion remains in direct conflict with the IPER, which had AL591783 before it: “The present application relates to a vitamin B6 phosphate phosphatase ... ***which has not been disclosed before in the prior art.***” (emphasis added) (Form PCT/Separate Sheet/409 (Sheet 1)); see also Form PCT/PEA/409 (concluding that all claims have novelty, inventive step, and industrial applicability).

The Examiner’s assertions are also in conflict with his conclusions in the enablement rejection – namely that “even small amino acid changes result in enzymatic activity changes.” (Paper No. 20070206 at 10.) It is respectfully submitted that the Examiner cannot have it both ways. Here, the overwhelming evidence is that Capela does not disclose what is claimed.

For this further reason, the rejection has been rendered moot and should be withdrawn.

**Rejection Under 35 USC § 103:**

Claims 2, 4, 7, and 11 were rejected under 35 USC § 103 as being unpatentable over Capela in view of Jang *et al.*, "*Human pyridoxal phosphatase. Molecular cloning, functional expression, and tissue distribution*," J. Biol. Chem., 2003 December 12, 278(50): 50040-46 ("Jang"). (Paper No. 20070206 at 12).

The rejection respectfully is traversed. At the outset we note that all arguments made in this paper concerning the §102 rejection are readopted and reasserted with respect to this rejection as if fully set forth here.

Capela is summarized above.

Jang discloses that "Pyridoxal 5' -phosphate (PLP) is the coenzymatically active form of vitamin B<sub>6</sub> and plays an important role in maintaining the biochemical homeostasis of the body (1,2)." (Page 50040, Col. 1). Jang further discloses that "[t]he PLP phosphatase cDNA was cloned between the BamHI of the bacterial expression vector pQE30 (Qiagen) after PCR amplification. Transformants of *E. coli* M15/pRER4 with the resulting pQE30-hPLPP construct were grown at 37°C in 200 ml of LB medium with 100 µg/ml ampicillin and 25 µg/ml kanamycin. The plasmid pREP4 constitutively expresses the Lac repressor protein encoded by the *lacI* gene to reduce the basal level of expression (Quiagen). When that culture had grown to an A<sub>600</sub> of 0.6, isopropyl β-D-thiogalactopyranoside was added to a final concentration of 1mM. After inducing the expression of the PLP phosphatase protein for 16 h at 25°C cells were harvested, washed, and resuspended in 20 ml of 20 mM Tris-HCl buffer, pH 7.4, containing 200 mM NaCl and 20 mM imidazole." (Page 50041, Col. 1).

In making the rejection, the Examiner asserted that Capela discloses “a DNA, which encodes a putative oxidoreductase type protein, [that] is 99.5% identical to SEQ ID NO: 9 of the instant application, inherently a vitamin B6 phosphate phosphatase protein.” (Paper No. 20070206 at 12).

The Examiner acknowledged, however, that Capela “do[es] not teach a vector comprising said sequence, [a] transformed host cell and a method of producing said protein in [a] transformed host cell and extraction of cell lysate.” (*Id.*).

To fill the acknowledged gap in Capela, the Examiner relied on Jang for “teach[ing] human pyridoxal phosphatase or vitamin B6 phosphate phosphatase, its molecular cloning in a vector, functional expression in [an] *E. coli* host cell, and [a] process for producing said protein followed by extraction and purification (p50041, col. 1).” (*Id.* at 13).

The Examiner then contended that “[i]t would have been obvious to one [of] ordinary skill in the art at the time of the invention ... to combine the teachings of Capela et al. and Jang et al. to clone the DNA of Capela et al. in a vector, transform an *E. coli* host cell, a process for producing said protein in *E. coli* cells, extract the cell lysate and purification by using the teaching of Jang et al.” (*Id.*).

With a view toward furthering prosecution, we note that claim 2 has been cancelled, without prejudice, and incorporated into non-rejected amended claim 1. Claim 11 has been amended to depend from non-rejected amended claim 1. Therefore, the rejection is moot as to claims 2 and 11. Claims 4 and 7 are the only remaining claims rejected.

Claim 4 (from which claim 7 depends) has been amended to recite “[a] recombinant microorganism of the genus *Sinorhizobium* or *Escherichia*, capable of producing vitamin B<sub>6</sub> from vitamin B<sub>6</sub> phosphate, wherein said microorganism is transformed with a DNA encoding vitamin B<sub>6</sub> phosphate phosphatase selected from the group consisting of:

- (a) a DNA sequence of SEQ ID NO:9;
- (b) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity and hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof;
- (c) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity, wherein said polypeptide is at least 70% identical to the amino acid sequence of SEQ ID NO:10;
- (d) a DNA sequence encoding a polypeptide having vitamin B<sub>6</sub> phosphate phosphatase activity and is at least 70% identical to the DNA sequence of SEQ ID NO:9; and
- (e) a degenerate DNA sequence of any one of (a) to (c).”

It is well settled that the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO should include evidence relevant to

the finding of whether there is a teaching, motivation, or suggestion to select and combine the documents relied on by the Examiner as evidence of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731-32 (2007) (the obviousness “**analysis should be made explicit**” and the teaching-suggestion-motivation test is “**a helpful insight**” for determining obviousness) (emphasis added); *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). Moreover, the factual inquiry whether to combine documents must be thorough and searching. And, as is well settled, the teaching, motivation, or suggestion to combine “**must be based on objective evidence of record.**” *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (emphasis added).

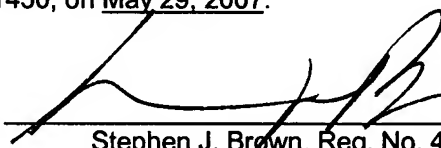
Initially, we note that Jang is not properly cited as prior art against the present claims. The Examiner acknowledged the present application’s claim to benefit to International application no. PCT/EP2003/010575, which claims benefit to EP application no. 02021622.2 filed on September 27, 2002. (Paper No. 20070206 at 4). Here, the Jang reference was published in the December 12, 2003 issue of the J. Biol. Chem. - over one year *after* the priority EP application was filed. In view of the foregoing, the Jang reference cited by the Examiner is not prior art to the present application. Because the rejection has failed to fill the acknowledged gaps in Capela, it is insufficient as a matter of law and must be withdrawn.



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Amendment Dated: May 29, 2007  
Reply to Office Action Dated: February 28, 2007

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the objections and rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on May 29, 2007.

  
Stephen J. Brown, Reg. No. 43,519

Respectfully submitted,

By: 

Stephen J. Brown  
Registration No. 43,519  
BRYAN CAVE LLP  
1290 Avenue of the Americas  
33<sup>rd</sup> Floor  
New York, NY 10104-3300  
Phone: (212) 541-2000  
Fax: (212) 541-4630